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TORYS LLP
79 WELLINGTON ST. WEST
SUITE 3000
TORONTO, ON M5K 1N2
CANADA

EXAMINER	
ROMEO, DAVID S	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/718,526	TAM, CHERK SHING	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *14-17 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-17 and 20-25* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0404*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 10/13/2006 has been entered. Claims 1–17 and 20–25 are pending.

Applicant's election of claims belonging to Group I, which encompasses claims 1 to 13 and 23 to 25 insofar as they relate to polypeptides which promote bone growth and having amino acid sequences identified as SEQ ID NO:12, amino acids 6 to 16 of SEQ ID NO:13, and SEQ ID NO:19, subsequences thereof, conservatively substituted variants thereof, and amino acid sequences encoded by a first nucleic acid molecule which hybridizes with a second nucleic acid molecule under high stringency hybridization conditions the complementary coding strand of which second nucleic acid molecule encodes a polypeptide consisting of 8 to 13 consecutive amino acids selected from the amino acid sequence identified as SEQ ID NO:12 in the reply filed on 10/13/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 14–17 and 20–22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/13/2006.

Applicant's election with traverse of polypeptide species based on SEQ ID NO:19, which encompasses claims 1 to 13 and 24 in the reply filed on 10/13/2006 is acknowledged. The traversal is on the ground(s) that claim 1 includes amino polypeptides based on the 11-amino acid sequence of amino acids 6 through 16 of SEQ ID NO:13 which includes SEQ ID NO:19 as a subsequence; that claims 23 and 25 are based on SEQ ID NO:12, a 14-amino acid sequence polypeptide which includes SEQ ID NO:19 as a subsequence; that further, the 11-amino

sequence of SEQ ID NO:13 is identical to amino acids 3 through 13 of SEQ ID NO:12 save for one amino acid; that as such, Applicant believes that it should be entitled to protection across the full scope of these claims; that there would be no serious burden on the Examiner to search across the full scope of these claims; that setting search parameters to cover all sequences of the generic claims is readily achievable; that further, the Commissioner has stated that a reasonable number of sequences may be claimed in a single application. Applicants respectfully submit that the two longer sequences, and the subsequences thereof, recited in the claims at issue amount to a reasonable number, particularly in view of their relationship to each other. This is not found persuasive because the examiner did not make a species election requirement and because such arguments are not germane to the restriction between groups I and II.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1–13 and 23–25 are being examined.

Claim Objections

Claim 1 is objected to because of the following informalities: Claim 1 ends in a double period. Claims should end in a single period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1–6, 13 and 23-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide selected from: (i) a polypeptide consists of 8 to 13 consecutive amino acids selected from the amino acid sequence identified as SEQ ID NO:12 and containing the sequence identified as SEQ ID NO: 19, and (ii) a polypeptide consisting of up to 13 consecutive amino acids selected from the amino acid sequence identified as SEQ ID NO:13 and containing amino acid sequence of 6 to 16 thereof, does not reasonably provide enablement for a conservatively substituted variant of (i) or (ii) which promotes bone growth in mammals or for an isolated polypeptide which promotes bone growth in mammals, the polypeptide comprising an amino acid sequence encoded by a first nucleic acid molecule which hybridizes with a second nucleic acid molecule under high stringency hybridization conditions, wherein high stringency conditions include a wash step of about 0.2x SSC at 50° C, the complementary coding strand of which second nucleic acid molecule encodes a polypeptide consisting of 8 to 13 consecutive amino acids selected from the amino acid sequence identified as SEQ ID NO:12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification teaches polypeptides consisting of an amino acid sequence selected from the group consisting of SEQ ID NO: 1, 2, 11, 12, 13, 17, 18 promote bone growth (Figure 5). The results with SEQ ID NO: 13 were questionable. The subsequences SEQ ID NO: 14 and 15 were found to have no effect on observed bone mineral apposition rate. See specification, paragraph 8. SEQ ID NO: 12 differs from all the other sequences by a single Q→E conservative amino acid substitution, which substitution lies outside of the subsequence SEQ ID NO: 19.

At their broadest, the claims are directed to or encompass conservatively substituted variants of SEQ ID NO: 19 and variants encompassed by the hybridization limitation of claim 23 of any 8 to 13 consecutive amino acids of SEQ ID NO: 12. There is no limit on the amount of conservative substitution. There is no limit on the number or type of amino acid substitutions encompassed by the hybridization language. The specification lacks working examples of, and accordingly, guidance for making, such variants of SEQ ID NO: 19. The examiner is aware working examples are not required. Lack of a working example is, however, a factor to be considered. Moreover, there is a lack of predictability in the art. Predicting structure, hence function, from primary amino acid sequence data is extremely complex and there doesn't exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. See Bowie (Science, (1990 Mar 16) 247 (4948) 1306-10) page 1306, column 1, full paragraph 1 or Ngo (The Protein Folding Problem and Tertiary Structure Prediction, Merz and Le Grand (Eds), August 1994, Springer Verlag, pages 433 and 492-495) page 433, full paragraph 1, and page 492, full paragraph 2. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, and the unpredictability in the art, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

Claims 1–6, 13 and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification teaches polypeptides consisting of an amino acid sequence selected from the group consisting of SEQ ID NO: 1, 2, 11, 12, 13, 17, 18 promote bone growth (Figure 5). The results with SEQ ID NO: 13 were questionable. The subsequences SEQ ID NO: 14 and 15 were found to have no effect on observed bone mineral apposition rate. See specification, paragraph 8. SEQ ID NO: 12 differs from all the other sequences by a single Q→E conservative amino acid substitution, which substitution lies outside of the subsequence SEQ ID NO: 19.

At their broadest, the claims are directed to or encompass conservatively substituted variants of SEQ ID NO: 19 and variants encompassed by the hybridization limitation of claim 23 of any 8 to 13 consecutive amino acids of SEQ ID NO: 12. There is no limit on the amount of conservative substitution. There is no limit on the number or type of amino acid substitutions encompassed by the hybridization language.

Vas-Cath Inc. v. Mahurkar , 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

With the exception of SEQ ID NO: 19, the skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of

isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGFs were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO: 19 but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115).

Claims 2–3 and 8–13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim

indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 2–3 and 8–13 recite the broad recitation "containing", which is synonymous with "comprising" and is therefore inclusive or open-ended and does not exclude additional, unrecited elements. Claims 2–3 and 8–13 depend directly or indirectly from claims 1 and 7. Claims 1 and 7 recite "consisting of" which is the narrower statement of the range/limitation because "consisting of" excludes any element, step, or ingredient not specified in the claim. A claim which depends from a claim which "consists of" the recited elements or steps cannot add an element or step. Therefore, it is unclear if the polypeptide of claims 2–3 and 8–13 comprises or consists of the recited elements. The metes and bounds are not clearly set forth.

Claims 4–6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 depends from an unspecified claim, and thus makes no sense, since it is incomplete. Claims 5–6 depend directly or indirectly from claim 4 and thus also share this defect. The metes and bounds are not clearly set forth.

Claims 23 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 recites "wherein high stringency conditions include a wash step of about 0.2x SSC at 50 °C". Although there are many differing methods of hybridization, they all comprise hybridization and washing following the hybridization. It is unclear what hybridization conditions are to be used. Claim 25 depends from claim 23 and also shares this defect. The metes and bounds are not clearly set forth.

Claims 7–12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the limitation "8 to 13 consecutive amino acids selected from the amino acid sequence identified as SEQ ID NO:12, SEQ ID NO:19, and containing the sequence identified as SEQ ID NO: 19." It is unclear how to interpret this limitation. Claims 8–12 depend directly or indirectly from claim 7 and thus also show this defect. The metes and bounds are not clearly set forth.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1–13 and 23–24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1–3 of U.S. Patent No. 6,693,081. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1–3 of the patent are directed to or encompass a polypeptide consisting essentially of SEQ ID NO: 18. The patent's specification defines SEQ ID NO: 18 as the sequence "Xaa Thr Ser Gly Ile His Pro Xaa" wherein the Xaas at positions 1 and 8 of SEQ ID NO: 18 are N-acetyl threonine and lysinamide, respectively.

SEQ ID NOs: 12, 13 and 19 of the present application all comprise the sequence "Thr Thr Ser Gly Ile His Pro Lys". Claims 24 and 25 of the present application define the presently claimed polypeptide as having both the N-terminal amino acid and the C-terminal amino acid protected by a protecting group. N-acetyl threonine and lysinamide are protected by a protecting group. Accordingly, the present claims are generic to and fully encompass the claims of the patent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 23 is rejected under 35 U.S.C. 102(b) as being anticipated by Baggiolini (WO 90/06321).

Baggiolini discloses the purification of NAP-2 (Example 3, pages 13-14).

SEQ ID NO: 12 of the present application is >95% identical to the corresponding amino acids of NAP-2, as indicated in the sequence comparison below:

```
R05767
ID   R05767 standard; protein; 128 AA.
AC   R05767;
DT   05-NOV-1990  (first entry)
DE   Precursor of platelet basic protein (PBP).
KW   Platelet basic protein; PBP;
KW   connective tissue-activating peptide III; CTAP-III;
KW   Beta-thromboglobin; Beta-TG;
KW   neutrophil stimulating activity; NSA-I;
KW   neutrophil activating peptide-1; NAP-1;
KW   psoriasis; arthritis; asthma; neutrophils; ds.
OS   Synthetic.
FH   Key             Location/Qualifiers
FT   disulfide_bond  63. .89
FT   disulfide_bond  65. .105
PN   WO9006321-A.
PD   14-JUN-1990.
PF   17-NOV-1989; 001389.
PR   8-DEC-1988; GB-028728.
PR   27-APR-1989; GB-009681.
PA   (KOCH-) Kochert Inst, (SANO) Sandoz Ag.
PI   Baggiolini M, Clemetson KJ, Walz A;
DR   WPI; 90-209750/27.
DR   N-PSDB; Q05141.
PT   New neutrophil-activating peptide-2 -
PT   useful in treatment of infections and inflammatory conditions.
PS   Disclosure; p; English.
CC   NAP-2 affects number and activation state of neutrophils, and
CC   as such is useful in treatment of bacterial, mycoplasma and fungal
CC   and viral infections. It is also useful in treatment of inflammatory
CC   diseases, eg. psoriasis, arthritis and asthma.
SQ   Sequence   128 AA;
```

```
  Query Match             95.8%;  Score 69;  DB 1;  Length 128;
  Best Local Similarity   92.9%;  Pred. No. 6.7e-06;
  Matches   13;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;
```

```
Qy       1 IKTTSGIHPKNIES 14
           |||||||||||||:|
Db      66 IKTTSGIHPKNIQS 79
```

The single amino acid difference can be accounted for by a single nucleotide substitution.

According to the present specification, NAP-2 shows bone stimulatory effects (paragraph 8).

Accordingly, Baggiolini discloses an isolated polypeptide which promotes bone growth in mammals, the polypeptide comprising an amino acid sequence encoded by a first nucleic acid molecule which hybridizes with a second nucleic acid molecule under high stringency hybridization conditions, wherein high stringency conditions include a wash step of about 0.2x SSC at 50° C, the complementary coding strand of which second nucleic acid molecule encodes a polypeptide consisting of 8 to 13 consecutive amino acids selected from the amino acid sequence identified as SEQ ID NO:12.

Claims 1–3, 7–13 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Whitman (U. S. Patent No. 5,470,831).

Whitman discloses an angiogenic peptide consisting of the amino acid sequence Thr-Thr-Ser-Gly-Ile-His-Pro-Lys and a pharmaceutical composition comprising same (column 16, claims 15-16). Certain residues are substituted by functionally equivalent amino acids resulting in a silent change. For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity which acts as a functional equivalent, resulting in a silent alteration. Substitutes for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar

(hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid. See column 3, lines 38-58.

The claimed polypeptide and Whitman's polypeptide are identical or substantially identical in structure or composition. Therefore, promotion of bone growth is presumed to be inherent, and a prima facie case of either anticipation or obviousness has been established. Applicant has the burden of distinguishing between the claimed polypeptide and Whitman's polypeptide.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 23–25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitman (U. S. Patent No. 5,470,831) as applied to claims 1 and 23 above, and further in view of Stout (U. S. Patent No. 5,635,371).

Whitman discloses an angiogenic peptide consisting of the amino acid sequence Thr-Thr-Ser-Gly-Ile-His-Pro-Lys and a pharmaceutical composition comprising same (column, 16, claims 15-16), as discussed above. Whitman does not teach, only in the sense that Whitman does not anticipate, an angiogenic peptide consisting of the amino acid sequence Thr-Thr-Ser-

Gly-Ile-His-Pro-Lys 24 wherein one or the other of the N-terminal amino acid and the C-terminal amino acid is protected by a protecting group or both of the N-terminal amino acid and the C-terminal amino acid are protected by protecting groups.

Stout discloses that modification of the N- and/or C-terminal amino acids of a peptide can result in the formation of analogs that are longer acting and more potent than the naturally occurring polypeptide (column 5, full paragraph 1). The unprotected terminal α-carbon reactive groups can be modified by reaction with a chemical modifying agent. Specific examples of types of modifications include: C-terminal amidation or formation of an N-acetyl group. Modification can occur at one or both terminal α-carbon reactive groups. See column 4, lines 38-48. Stout does not teach an angiogenic peptide consisting of the amino acid sequence Thr-Thr-Ser-Gly-Ile-His-Pro-Lys wherein one or the other of the N-terminal amino acid and the C-terminal amino acid is protected by a protecting group or both of the N-terminal amino acid and the C-terminal amino acid are protected by protecting groups.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make an angiogenic peptide consisting of the amino acid sequence Thr-Thr-Ser-Gly-Ile-His-Pro-Lys, as taught by Whitman, and to modify that teaching by C-terminal amidation or N-terminal acetylation, as taught by Stout, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because modification of the N- and/or C-terminal amino acids of a peptide can result in the formation of analogs that are longer acting and more potent than the naturally occurring polypeptide.

The invention is prima facie obvious over the prior art.

Specification

The disclosure is objected to because of the following informalities:

The application is not fully in compliance with the sequence rules, 37 C.F.R. § 1.821-1.825. Specifically, the specification fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. See, for example, the Abstract. This is not meant to be an exhaustive list of places where the specification fails to comply with the sequence rules. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The application cannot issue until it is in compliance. Nucleic acid sequences with 10 or more nucleotides, at least 4 of which are specifically defined, must comply with the sequence rules. Amino acid sequences with 4 or more residues, at least 4 of which are specifically defined, must comply with the sequence rules. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing."

Appropriate correction is required.

Conclusion

No claims are allowable.

5

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

10

DSR
JANUARY 3, 2007